

CLAIMS

1. A pellet comprising an acid labile benzimidazole compound, wherein the pellet comprises:

an inert nucleus; ^{a?}

5 a layer disposed over said inert nucleus (a), comprising an acid labile benzimidazole compound, an inert, non-alkaline polymer soluble in water and one or more pharmaceutically acceptable inert excipients;

one or more intermediate layers that comprise:

an inert, non-alkaline coating, formed of an inert, non-alkaline polymer soluble in water and one or more pharmaceutically acceptable inert excipients; and

a system of modified release that comprises an inert, non-alkaline polymer soluble in water and an inert, non-alkaline polymer insoluble in water; ^{LAP}

13 said intermediate layer(s) (c) disposed over said layer (b) that covers the inert nucleus; and ^{112 b?} ¹¹²

15 an external layer comprising an enteric coating disposed over said intermediate layer(s) (c).

20 2. A pellet according to claim 1, in which said intermediate layers (c) comprise one or more layers of an inert, non-alkaline coating and one or more layers of a system of modified release that comprises an inert, non-alkaline polymer soluble in water and an inert, non-alkaline polymer insoluble in water.

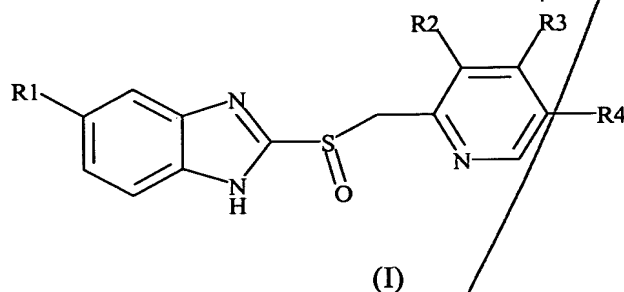
25 3. A pellet according to claim 1, wherein, the inert, non-alkaline coating, formed of an inert, non-alkaline polymer soluble in water and one or more pharmaceutically acceptable inert excipients, and the system of modified release that comprises an inert, non-alkaline polymer soluble in water and an inert, non-alkaline polymer insoluble in water, are mixed in a single layer.

30 4. A pellet according to claim 1, in which said intermediate layers (c) comprise a mixture of one or more layers of inert, non-alkaline coating, and one or more layers of said system of modified release that comprises an inert, non-alkaline polymer soluble in water and an inert, non-alkaline polymer insoluble in water, and one or more layers of a mixture of inert, non-alkaline coating, and said system of modified release that comprises an inert, non-alkaline polymer soluble in water and an inert, non-alkaline polymer insoluble in water.

35 5. A pellet according to claim 1, wherein the inert, non-alkaline coating, formed of an inert, non-alkaline polymer soluble in water and one or more pharmaceutically acceptable inert excipients is disposed over the layer (b); the layer comprising the system of modified release that comprises an inert, non-alkaline polymer soluble in water and an inert, non-alkaline polymer insoluble in water is disposed over the layer of the inert, non-alkaline

coating; and the layer (d) is disposed over the layer formed by the system of modified release comprising an inert, non-alkaline polymer soluble in water and an inert, non-alkaline polymer insoluble in water.

6. A pellet according to claim 1, wherein said acid labile benzimidazole compound is a compound of formula (I)



wherein

R^1 is hydrogen, methoxy or difluoromethoxy,

R^2 is methyl or methoxy,

R^3 is methoxy, 2,2,2-trifluoroethoxy or 3-methoxypropoxy, and

R^4 is hydrogen or methyl.

7. A pellet according to claim 1, wherein said acid labile benzimidazole compound is selected from the group consisting of omeprazole, lansoprazole and pantoprazole.

8. A pellet according to claim 1, wherein, said inert, non-alkaline polymer soluble in water, present in the layer (b) is selected from hydroxypropylmethylcellulose (HPMC) and hydroxypropylcellulose (HPC).

9. A pellet according to claim 1, wherein, said inert, non-alkaline polymer soluble in water of the inert, non-alkaline coating, present in the intermediate layer(s) (c) is hydroxypropylmethylcellulose (HPMC).

10. A pellet according to claim 1, wherein, said inert, non-alkaline polymer soluble in water of the system of modified release, present in the intermediate layer(s) (c) is hydroxypropylmethylcellulose (HPMC).

11. A pellet according to claim 1, wherein, said inert, non-alkaline polymer insoluble in water of the system of modified release, present in the intermediate layer(s) (c) is ethylcellulose or a copolymer of ammonium methacrylate.

12. A pellet according to claim 1, wherein, said external layer (d) comprises a gastro-resistant polymer, a plasticizer and one or more pharmaceutically acceptable inert excipients.

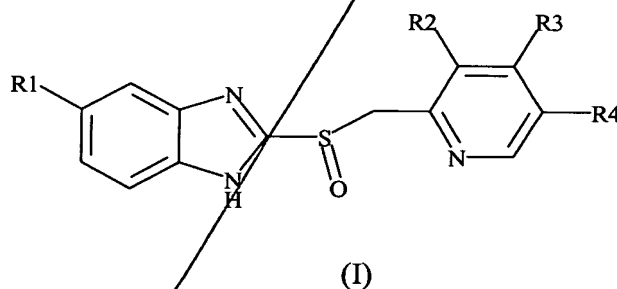
13. A method for obtaining a gastro-resistant pellet of modified release that contains as an active ingredient an acid labile benzimidazole compound, that comprises:

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 (i) applying an aqueous suspension of an acid labile benzimidazole compound, an inert, non-alkaline polymer soluble in water, and one or more pharmaceutically acceptable inert excipients to cover an inert nucleus;

(ii) applying one or more intermediate layers, separated or mixed among themselves that contain (i) an inert, non-alkaline coating, formed of an inert, non-alkaline polymer soluble in water and one or more pharmaceutically acceptable inert excipients; and (ii) a system of modified release that comprises an inert, non-alkaline polymer soluble in water and an inert, non-alkaline polymer insoluble in water, a plasticizer and an anti-tack agent, separated or mixed; and

(iii) covering said intermediate layer or layers with an aqueous suspension that comprises a gastro-resistant polymer, a plasticizer and one or more pharmaceutically acceptable inert excipients to create an external layer of enteric coating.

14. A method according to claim 13, wherein said acid labile benzimidazole compound is a compound of formula (I)



wherein

R¹ is hydrogen, methoxy or difluoromethoxy,

R² is methyl or methoxy,

R³ is methoxy, 2,2,2-trifluoroethoxy or 3-methoxypropoxy, and

R⁴ is hydrogen or methyl.

15. A method according to claim 13, wherein said acid labile benzimidazole compound is selected from the group consisting of omeprazole, lansoprazole and pantoprazole.

16. A method according to claim 13, wherein, said inert, non-alkaline polymer soluble in water, present in the suspension applied in step (i) is selected from hydroxypropyl-methylcellulose (HPMC) and hydroxypropylcellulose (HPC).

17. A method according to claim 13, wherein, said inert, non-alkaline polymer soluble in water, comprised in the inert, non-alkaline coating, present in the suspension applied in step (ii) is hydroxypropylmethylcellulose (HPMC).

18. A method according to claim 13, wherein, said inert, non-alkaline polymer soluble in water, comprised in the system of modified release, present in the suspension applied in step (ii) is hydroxypropylmethylcellulose (HPMC).
19. A method according to claim 13, wherein, said inert, non-alkaline polymer insoluble in water, comprised in the system of modified release, present in the suspension applied in step (ii) is ethylcellulose or a copolymer of ammonium methacrylate.
20. A composition of modified release that comprises one or more pellets of claim 1.
21. A composition according to claim 20, in which one or more of the pellets have the same release profile of the benzimidazole.
- 10 22. A composition according to claim 20, in which one or more of the pellets have a different release profile of the benzimidazole.
23. A composition according to claim 20, comprising a mixture of (i) pellets with a quick release profile and (ii) pellets with a slow release profile, in a ratio (i):(ii), by weight, lying between 10:90 and 90:10.
- 15 24. A composition according to claim 20, in the form of a capsule or a tablet.

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